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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/769,107	01/24/2001	Vincent P. Sandanayaka	WYTH0144-100/AM100182 01	4495

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EXAMINER	
COVINGTON, RAYMOND K	
ART UNIT	**PAPER NUMBER**
1625	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/769,107	SANDANAYAKA ET AL.	
	Examiner	Art Unit	
	Raymond Covington	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,29-31,33-39,45-49 and 53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14,29-31,33-39,45-49 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-14, 29-31, 33-39, 45-53 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Levin et al WO 00/44723. Levin et al teach a method of making alpha sulfone ester derivative as recited in the claims. See, for example, page 66, example 24 corresponding to compounds where Z is ethyl and page 68 example 25 where Z is chlorobenzyl.

Please note that § 102(e) date of Levin et al is the earliest U.S. filing date for which a benefit is properly sought via §§ 119(e) and/or 120.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14, 29-31, 33-39, 45-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-14, 29-31, 33-39, 45-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling compounds of formula I, V and IX where R_1 R_2 taken together with the carbon atom to which they are attached form a piperidine ring, Z is CH_3-CH_2-O-, OH-NH-, OH or CH_3-O-, and R_3 is a phenyl group, does not reasonably provide enablement for the broader scope in claims dependent thereon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. Specification provides no guidance as to what other rings, for example, might be suitable and there is no

basis in the prior art directed to similar compounds having the same activity as herein.

The Wands factors are again applied as set forth in the previous office action. Applicants' comments have been noted and considered but are not deemed persuasive of patentability.

There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and further would not be produced by the same process. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

There is insufficient disclosure of starting materials that would place such a diverse genus of compounds in possession of the public in the event of a patent grant. The limited number of examples do not enable the preparation of such a diverse group the compounds embraced by the claims as presently recited, e.g. where Y, R_1 and R_2 are 10 member trioxo containing heterocyclic rings verse where Y is hydrogen R_1 and R_2 are cyclohexyl.

There is insufficient disclosure of starting materials that would place such a diverse genus of compounds in possession of the public with a reasonable assurance that such an alleged genus of compounds could be made by the same

process. See In re Fouche 169 USPQ 429 ((CCPA 1971)). This is particularly true where large groups such as heteroaryl may sterically hinder or may prevent the making of the starting materials, intermediates or final products.

Applicants' reference to pages 24, 31-72 of the specification for exemplification is noted, however, it does not disclosed any working examples, which would demonstrate, or guide, one skilled in the art as to how the heterocyclic substituted or other substituent groups other than where R_1 R_2 taken together with the carbon atom to which they are attached form a piperidine ring, Z is CH_3-CH_2-O-, OH-NH-, OH or CH_3-O-, and R_3 is a phenyl group were prepared or obtained. The process of making the recited compounds is not readily apparent from the specification. The specification must teach how to make the invention. *In re Gardner*, 166 U.S.P.Q. 138 (1970). In order to practice the claimed invention, one skilled in the art would have speculate how the derivatives were obtained or prepared.

Accordingly, the rejection is maintained.

Claim 46 is rejected to the extent it reads on and depends from a rejected base claim.

Claims 48 and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for treating any disease

or condition. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims.

The Wands factors are applied as in the previous office action. Applicants' comments have been noted and considered but are not deemed persuasive of patentability.

The claim provides for the use of claimed compounds, but the claim does not set forth any steps involved in determining which are the "disease states associated with inhibiting pathological changes mediated by TNF-alpha converting enzymes (TACE)". It is unclear which diseases are "associated with inhibiting pathological changes mediated by TNF-alpha converting enzymes (TACE)." Determining whether a given disease responds or does not respond to such an enzyme and thus, is covered by the claim language, can only be accomplished through potentially inconclusive clinical research. Suppose that a given drug, which has enzyme inhibiting properties *in vitro*, when administered to a patient with a certain disease, does not produce a favorable response. One cannot conclude that specific disease does not fall within this claim. Keep in mind that:

A. It may be that the next patient will respond. No pharmaceutical has 100% efficacy. What success rate is required to conclude our drug is a treatment? Thus, how many patients need to be treated? If "successful treatment" is what is

intended, what criterion is to be used? If one person in 10 responds to a given drug, does that mean that the disease is treatable? One in 100? 1,000? 10,000? Will the standard vary depending on the current therapy for the disease?

B. It may be that the wrong dosage or dosage regimen was employed. Drugs with similar chemical structures can have markedly different pharmacokinetics and metabolic fates. It is quite common for pharmaceuticals to work and or be safe at one dosage, but not at another that is significantly higher or lower. Furthermore, the dosage regimen may be vital --- should the drug be given e.g. once a day, or four times in divided dosages? The optimum route of administration cannot be predicted in advance. Should our drug be given as a bolus *iv* or in a time-release *po* formulation. Thus, how many dosages and dosage regimens must be tried before one is certain that our drug is not a treatment for this specific disease?

C. It may be that our specific drug, while active *in vitro*, simply is not potent enough or produces such low concentrations in the blood that it is not an effective treatment of the specific disease. Perhaps a structurally related drug is potent enough or produces high enough blood concentrations to treat the disease in question, so that the first drug really does fall within the claim. Thus, how many

different structurally related receptor antagonists must be tried before one concludes that a specific disease does not fall within the claim?

D. Conversely, if the disease responds to our second drug but not to the first, both of whom are enzyme inhibiting *in vitro*, can one really conclude that the disease falls within the claim? It may be that the first compound result is giving the accurate answer, and that the success of second compound arises from some other unknown property that the second drug is capable. It is common for a drug, particularly in the CNS, to work by many mechanisms. The history of psychopharmacology is filled with drugs, which were shown to effect a variety of biological targets. In fact, the development of a drug for a specific disease and the determination of its biological site of action usually precede linking that site of action with the disease. Thus, when mixed results are obtained, how many more drugs need be tested?

E. Suppose that our drug is an effective treatment of the disease of interest, but only when combined with some very different drug. There are for example, agents in antiviral and anticancer chemotherapy that are not themselves effective, but are effective treatments when the agents are combined with something else.

F. Even the most desired outcome does not unequivocally establish the meaning of the phrase. Our drug alone could be an effective treatment of the

disease of interest. One still cannot conclude that the disease cured is a "Factor X enzyme inhibited disease". What if our drug has a second biological effect in addition to Factor Xa enzyme inhibition? It is possible that this second mechanism is responsible for the positive outcome.

Consequently, determining the true scope of the claim will require potentially inconclusive research. Without it, one skilled in the art cannot determine the actual scope of the claim. Hence, the claim is indefinite.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 is unclear. Defining a disease by its (their) underlying cause renders the scope of intended uses indeterminate since the claim language may read on diseases not yet known to be caused by or affected by such action or in ways not yet understood.

Claims 1 and 2 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims do not positively recite the method

steps of the claimed process. There is not recitation of how formula V is converted to formula I, the final product.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie at telephone number (571) 272-0681.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Thomas McKenzie
SPE
Art Unit 1625